REMARKS

Claims 1-14, 17-23, 64-76 were pending in the instant application. By this amendment, claims 1, 4, 5, 12-14, 17-19, 21, 64, 67, 68-74, 76 and 79 have been amended to to present rejected claims in form for allowance and/or consideration on appeal, and claims 65 and 66 have been canceled, without prejudice to applicants' right to pursue the subject matter of the canceled claims in other applications. In particular, claims 4, 5, 12, 68, 69-74 and 79 have been amended to clarify the invention and to correct inadvertent clerical errors; claims 1, 13, 14, 17, and 21 have been amended to specify that the α2M receptor activity is an HSP binding, HSP uptake, or HSP-mediated antigen representation activity; claims 18, 19, 64, 67, 68, 76 have been amended to include ligand-binding fragments of the α2M receptor; and claims 72-74 have been amended to clarify that to "stimulate the activation of" cytotoxic T cells means to "activate" cytotoxic T cells. Support for the amendments can be found throughout the specification as originally filed (see, *e.g.*, the specification at page 10, lines 26-34, page 27, lines 20-28; page 32, lines 18-23). As such, no new matter has been added.

Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS SHOULD BE WITHDRAWN

Claims 1 and 68 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite in the recitation of the phrase "receptor-mediated process." In particular, the Examiner contends that the α2M receptor has many other functions not associated with the interaction with HSPs, and that the phrase "receptor-mediated processes," reads on such other non-HSP-related receptor functions. Applicants respectfully submit that the rejection is in error for the reasons set forth below.

The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Orthokinetic Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986). Thus, according to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985).

Applicants respectfully submit that the Examiner has taken the term "receptor-mediated process" out of context. Correctly interpreted, the phrase is understood as "HSP-α2M receptor-mediated process," and not isolated from its modifier "HSP-α2M," as the Examiner has done. The specification distinctly defines an "HSP- α2M receptor-mediated process" at page 10, lines 26-34 as follows:

> The term "HSP-α2M receptor-mediated process" as used herein refers to a process dependent and/or responsive, either directly or indirectly, to the interaction of HSP with the α2M receptor. Such processes include processes that result from an aberrant level of expression, synthesis and/or activity of α2M receptor, such as endocytic activities relating to the binding of the various α2M ligands, including but not limited to HSP, α2M, lipoprotein complexes, lactoferrin, tissue-type plasminogen activator (tPA), urokinase-type plas minogen activator (uPA), and exotoxins. Such processes include, but are not limited to, endocytosis, antigen presentation, cholesterol regulation, apoE-containing lipoprotein clearance, and chylomicron remnant removal.

As stated therein, HSP-α2M receptor-mediated processes directly or indirectly depend and/or are responsive to the interaction of HSP with the α2M receptor.

In addition, the meaning of the phrase "HSP-α2M receptor-mediated process" is further illustrated in the specification at page 33, line 35 through page 34, line 9, where antigen presentation assays are described which are dependent on HSP-α2M receptor interactions, and at page 38, lines 23-31, where assays designed to identify compounds that

effect α2M receptor-HSP interactions are defined. Thus, one skilled in the art, given the disclosure and teachings of the specification, would clearly understand the phrase "HSP-α2M receptor-mediated process," when read in light of the specification, to mean a process directly or indirectly resulting from interaction of the α2M receptor and an HSP, not any other α2M receptor-mediated processes. As such, the claimed methods do not read on functions which are not associated with the HSP-α2M receptor binding complex.

Nevertheless, claims 1 and 68 have been amended to require that the HSP-α2M receptor-mediated process be specific to an HSP-α2M receptor interaction, and not any other receptor-mediated process. In particular, the claimed methods identify compounds by measuring HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity. Thus, the methods require that the HSP-α2M receptor-mediated process depend on the interaction of an HSP with the α2M receptor, and not other non-HSP mediated α2M receptor-mediated processes. As such, one of skill in the art would clearly understand that the claimed invention does not encompass non-HSP-α2M receptor-mediated processes.

For all the foregoing reasons, Applicants respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 1-14, 17-23, and 64-76 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends that the specification does not adequately describe the genus of ligand-binding α2M receptor fragments, because, according to the Examiner, the specification does not adequately

describe binding fragments of α2M receptor because one skilled in the art would not be able to envision the detailed structure of fragments of the α2M receptor given the description of the specification. Applicants respectfully disagree and assert that the specification as filed provides adequate written description support for the claimed methods, which do not require a detailed structure of every species of the genus of α2M receptor ligand-binding fragments, for the reasons set forth below.

According to the relevant case law, a claimed genus must be supported by a description of relevant identifying characteristics of a representative number of species. *Regents of University of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied 523 U.S. 1089 (1998). What constitutes a "representative number of species" depends upon the knowledge and skill in the art. Moreover, such a description need not be sufficient to provide support to claim each individual species encompassed by the genus. The description is deemed sufficient if it demonstrates to the skilled artisan that the applicant was in possession of the necessary common attributes of the members of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405.

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, pages 1099-1111), specifies that an applicant may show that an invention is complete by "disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention." (*Id.* at page 1106, column 1, lines 22-33). According to the Guidelines, for each claimed genus, the test requires determination of whether there is sufficient description of

> . . .a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function

> and structure, or some combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus.
>
> *Id.* at page 1106, col. 3, lines 12-29

According to the Guidelines, there are situations where description of even one species adequately supports a genus. "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (*Id.* at page 1106, col. 3, lines 42-50).

The instant claims are directed to screening methods for identifying compounds that modulate the interaction of an HSP with the α2M receptor. Based on the discovery by the Applicants that HSPs interact with the α2M receptor, applicants invented the claimed assays which can be used to identify compounds useful for modulating the immune response. As described in the instant specification, the methods can be carried out with the full-length α2M receptor, or any portion of the α2M receptor that is capable of binding to an α2M-ligand, *e.g.*, an HSP. In this regard, the specification describes both specific structural and functional characteristics and representative species of the genus of ligand-binding fragments of the α2M receptor. For example, at page 12, line 32-33, an 80kDa fragment of the receptor that binds to an HSP is disclosed. The structure of the fragment is described by the exact amino acid residues of the fragment which are highlighted in bold in Figure 8A. Furthermore, at page 3, lines 23-26 cluster regions with binding domains of the α2M receptor are disclosed. In particular, Cluster II is designated as a ligand-binding domain. In addition, at page 4, lines 14-21, ligand-binding fragments are defined based on RAP binding to α2M receptor.

Moreover, the specification provides numerous functional assays that the skilled artisan could use to readily determine additional members of the genus of α2M

receptor ligand-binding fragments. In this regard, methods for identifying fragments of the α2M receptor that bind HSPs are described in Section 5.3 (see page 38, lines 13-27) where it is also taught that many of the assays described in Sections 5.2.1 and Section 5.2.2 can be utilized to identify ligand binding fragments of the α2M receptor. For example, in these sections, assays such as *in vivo* binding assays (page 28, line 18 through page 32, line 15), re-presentation assays (page 33, line 35 through page 34 line 9), and CTL assays (page 34, lines 10-29) are described which can be used to test the activity of HSP-binding fragments of the α2M receptor.

According to the relevant case law and the Guidelines discussed above, where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced. Here, armed with the description of numerous ligand-binding domain fragments, two specific working examples of ligand-binding α2M receptor sequences, as well as the structural characteristics and functional characteristics of other members of the genus, the skilled artisan would recognize that the applicant was in possession of the necessary common attributes of the genus, *i.e.*, α2M receptor sequences having the ability to bind an HSP, in view of the species disclosed.

The Examiner based his rejection on case law which discussed written description requirements in the context of claiming compositions of nucleic acids. The Examiner relied on *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), wherein the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. Applicants respectfully point out that this case law is not entirely applicable to the instantly claimed invention. *Eli Lilly* concerns the attempt to claim a genus based merely on a single species and the functional activity of other unknown sequences. In this case, in

amino acid sequences of the α2M receptor are well known in the art and disclosed in the instant application, together with sequences which comprise the ligand-binding portions thereof. Moreover, two species of the genus of ligand-binding α2M receptors are disclosed in the instant application, *i.e.*, the isolated α2M receptor and the 80kDa fragment thereof. Thus, ligand-binding fragments of the α2M receptor useful in the claimed assays are adequately described in the specification, both structurally and functionally, so that the skilled artisan would recognize that the applicants were in possession of the claimed invention, *i.e.*, assays for identifying compounds that modulate the interaction of an HSP with the α2M receptor.

In light of the foregoing reasons, the rejection under 35 U.S.C. § 112, first paragraph for lack of written description should be withdrawn.

CONCLUSION

Applicants respectfully request that the present remarks be entered and made of record in the instant application. It is submitted that the foregoing amendments and arguments made herein place the claims in condition for allowance. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

It is believed that no fee is required for filing this amendment. In the event a fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: May 5, 2003

Adriane M. Antler — 32,605
Adriane M. Antler (Reg. No.)

By: Eileen E. Falvey — 46,097
Eileen E. Falvey (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosures